

FURACA #10

AIM: Preparation of FURACA from ZACA by New Route

STAGE-I: PREPARATION OF ~~TFA~~ TFA (STD).

Raw Materials:

NaSH : 37.5g

DMW : 365.0g +

2. Furoyl Chloride : 27.5g

EtoAc : (250+100) ml

NaHCO<sub>3</sub> : 20.0g

DMW : 175.0 ml

~~Conc HCl~~ 1:1 HCl : (48+49) ml

PROCEDURE:

1. Charge DMW, cool to  $25-20^{\circ}\text{C}$ .
2. Charge NaSH and stir 5' to get clear sol<sup>n</sup>.
3. Add Furoyl chloride in 40-45' at  $20-25^{\circ}\text{C}$  and then stir 10' at same temp. +
4. Then charge EtoAc (250ml) and adjust the pH to 0.9-1.0 with 1:1 HCl at  $22-25^{\circ}\text{C}$  in 15'.
5. Separate the layers. Eliminate the aq. phase.
6. To the org. phase charge DMW (175) and adjust the pH to 7.0-7.1 with NaHCO<sub>3</sub> at  $20-22^{\circ}\text{C}$  in 15'.
7. Then stir for 30' at  $20-22^{\circ}\text{C}$  and separate the layers.
8. To the rich aq. layer- charge 100 ml EtoAc and again adjust the pH to 0.9-1.0 with 1:1 HCl at  $20-22^{\circ}\text{C}$  in 15'.
9. Stir 15' at  $20-22^{\circ}\text{C}$  and separate the layers.
10. This Org. layer (OL<sub>2</sub>) is taken for next stage.

Vol. of OL<sub>2</sub> (TFA) : ~~25~~ 130.0 ml

HPLC TFA Imp.

OL<sub>1</sub> 97.34 (1.0+1.0)

OL<sub>2</sub> 97.48 2.1

## STAGE-II: FURACA PREPARATION:

Mati : (A) STD. + EtOAc slurry <sup>and spray</sup> given separately.

(B) pH is adjusted to 3.0 only and the Net cake was washed with EtOAc slurry and spray.

### Raw Materials:

TACA : 50.0 g  
EtOAc : 200.0 g  
GAA : 30.0 ml  
BF<sub>3</sub> gas : 68.5 g.  
TFA sol<sup>n</sup> : 130.0 ml.  
EDTA : 0.3 g.

### Run. mass

	(A)	(B)
DMW	75.0 ml	75.0 ml
EDTA	0.15 g	0.15 g
SHS	0.5 g	0.5 g
18-20% NH <sub>3</sub> sol <sup>n</sup>	48.0 ml 2.5 pH	42.0 ml 3.0 pH
DMW	(45+75+25) ml	(25+75+25) ml
EtOAc	(75+25) ml	(75+25) ml

### PROCEDURE:

1. Charge EtOAc, GAA at RT and cool to 0°C.
2. Purge BF<sub>3</sub> gas at <10°C.
3. Add EDTA and stir 35' at 15°C.
4. Then charge TACA + stir for 5' and then charge TFA sol<sup>n</sup>.
5. Stir of the Run. mixture at 30°C for 2½ hr. & monitor the Run. mass.  
Divide the mass into two equal parts.

- Chave
- (A) ① To the one part into the precooled DMW (~~75%~~ for  $15^{\circ}\text{C}$ ) and add EDTA + SHS.
- ② Adjust the pH to 3.5 by 18-20%  $\text{NH}_3$  soln in 40-45' at ~~20~~  $25-30^{\circ}\text{C}$ .
- ③ Stir for 30' at  $25^{\circ}\text{C}$  and then filter it.
- ④ Wash the product with DMW spray, slurry & spray.
- ⑤ Take the wet cake in a RBF and add 75ml and stir for 15' at ~~2000~~  $25^{\circ}\text{C}$  and then filter.
- ⑥ Then give 25ml EtOH spray.
- ⑦ Dry the product at  $30-35^{\circ}\text{C}$  for 2hr-3hr.
- ⑧ Quantify the ~~Washing~~ EtOH layer.

- (B) ① Transfer the Rem. mass (another part) into the  $15^{\circ}\text{C}$  DMW and add EDTA + SHS.
- ② Adjust the pH to 3.0 by 18-20%  $\text{NH}_3$  soln in 40-45' at  $25-30^{\circ}\text{C}$ .
- ③ Stir for 30' at  $25^{\circ}\text{C}$  and then filter it.
- ④ Wash the product with DMW spray, slurry & spray.
- ⑤ Take the wet cake into the RBF and add 75ml EtOH and stir 15' at  $25^{\circ}\text{C}$ .
- ⑥ Filter it & wash with 25ml EtOH spray.
- ⑦ Dry it at ~~25~~  $35^{\circ}\text{C}$  for 2-3hr.
- ⑧ Quantify the Washing EtOH layer.

### R/M Results

Duration	TACA	FURACA	TFA	Pmp
1hr.	4.96	81.95	11.70	0.35
2hr.	0.74	89.86	7.81	0.33
2 1/2 hr.	0.20	91.26	7.10	

Terminated in 2 1/2 hr.

OBS: (1) TFA having 2% Impurity, even though  
 FURACA has gone smoothly.  
 (2) Colour of the Run mass is normal.  
 (3) While adding N<sub>2</sub>, the colour of  
 the slurry is somewhat different, it is  
 in greenish colour.  
 (4) In both case Rate of filtration is  
 normal & material nature also  
 same.

	Crude Net Wt	EtoAc slurry + spray	Dry Wt.
(A)	61.2 g	54.3 g	28.4 g
(B)	60.3 g	56.4 g	29.5 g

EtoAc slurry + spray washed, EtoAc layer Wt  
 % of FURACA  
 (A) Wt. of EtoAc only : 54.5g / 60.0ml  
 (B) Wt. of EtoAc only : 35.4g / 40.0ml

### HPLC Report

	FURACA	TACA	TFA	Imp	Cl
(A) Crude	97.37	0.35	1.17	0.31	
(B) Crude EtoAc washed	98.91	0.19	2.15	0.10	
(C) Crude EtoAc washed					

### Quantitative Analysis

	FURACA	MIC	% of FURACA in EtoAc
(A) Purified	91.93	2.1	0.0033 %
(B) "	81.84	2.01	0.0022 %